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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,099	10/31/2003	Dale B. Schenk	15270L-008930US	7805

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,099	SCHENK ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,54 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,54 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-6, 54 and 55 are under current examination.

In view of the Appeal Brief filed on 1/11/2010, PROSECUTION IS HEREBY REOPENED. A correction of citation in the applied reference and new grounds of rejection (Double Patenting rejections) are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Zachariah Lucas/
SPE, Art Unit 1648.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 54 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Ueda (*PNAS*, 1993- cited), US Patent No. 6093406, US Patent No.5583112 and US Patent No. 6172122.

The claims are drawn to (in part) a composition comprising an agent effective to elicit an immunogenic response to alpha-synuclein and an adjuvant that is pharmaceutically acceptable for human administration, wherein the adjuvant is selected from the group consisting of QS21, monophosphoryl lipid, alum, CpG, GM-CSF and M-CSF, wherein the agent is alpha-synuclein or an immunogenic fragment thereof (see claim 1).

Ueda et al describe the 35-amino acid peptide NAC (see whole document and [0006] of the instant specification disclosing an alpha-SN as an NAC or a non-Abeta component of AD amyloid). The authors describe the making of anti-NAC antibodies using 2 peptides (or fragments) dubbed X and Y used to raise rabbit antisera (see page

11283, col. 2, RESULTS and DISCUSSION). Note that the authors also conjugated the peptides to keyhole limpet hemocyanin by using MBS (see page 11282, MATERIALS and METHODS and instant claim 6). Thus, the authors provide a composition comprising NAC fragments which are conjugated and these conjugates are effective in eliciting an immunogenic response (i.e. antibody production), meeting the limitation of an "immunogenic alpha-synuclein fragments" (instant claim 4).

The authors do not describe using the adjuvants listed in instant claim 1, manufacturing such a composition under good manufacturing practice (instant claim 54) and filter sterilizing the agent (instant claim 55).

US Patent 6093406 describes liposomes comprising an antigen and lipid A and that are adsorbed to aluminum hydroxide or alum (see whole document, including col. 1, lines 10+ and instant claim 1). Col. 3, lines 42+ provide that it is generally expected that a vaccine prepared in accordance with Good Manufacturing Practices ("GMP") prescribed by the U.S. Food and Drug Administration will be less potent than one prepared otherwise. This expectation holds true for the above-described vaccine. Yet, the reduction in potency of the vaccine within the present invention is much less than that of a vaccine that comprises the antigen alone adsorbed to aluminum hydroxide.

US Patent 5583112 describes the immunogen activity of the saponin conjugates and saponin adjuvants, including QS-21 also known as QA-21 (see Detailed Description). Col. 5, lines 9+ recites the following: The increase in titer of

antibody against a particular antigen upon administration of the vaccines and/or adjuvants of the invention may be used as a criteria for immunogenic activity (Dalsgaard, K. (1978) Acta Veterinia Scandinavica 69:1-40, Scott et al. Int. Archs. Allergy Appl. Immun. 77:409-412 (1985)). Briefly, one such test involves injecting CD-1 mice intradermally with a saponin/antigen conjugate which may be mixed with varying amounts of a potential adjuvant. Sera was harvested from the mice two weeks later and tested by ELISA for anti-immunogen antibody. Note that the adjuvants are filtered including through a 0.2 mu nylon mesh (see Example 1) and this is taught throughout the disclosure. Thus, QS-21 is a known adjuvant which leads to an increase in antibody titer.

US Patent 6172122 provides the following recitation with respect to Good Manufacturing Practice (col. 21, lines 34+): In order for the compositions of this invention to be suitable for certain uses, compliance with FDA Good Manufacturing Practice (GMP) regulations (21 CFR Part 110) is required. GMP regulations specify a means to assure a clean product which is of purity suitable for its intended use, does not transmit biological disease agents and avoids adulteration. The regulations list specific and general requirements on cleanliness and suitability of personnel, utensils and equipment, operations, grounds and facilities and

measures to insure that processing controls are adequate. It is common practice for manufacturers to meet GMP with documented standard operating procedures (SOP) and check-lists and control charts to indicate compliance with the SOP on an hourly or daily basis, or on each batch as required.

It would have been obvious to one of ordinary skill in the art to combine the teachings above and incorporate known adjuvants in the composition taught by Ueda et al. One would have been motivated to do so for the advantage of increasing antibody titers by known adjuvants, including alum and QS-21, to an NAC fragment.

One would have also been motivated to abide by the GMP regulations to insure a purity suitable for its use as suggested above (US Patent 6172122). Further, the prior art teaches that GMP can lead to a reduction in potency of the composition and adjuvants may overcome this reduction by further amplifying an immune response (US Patent 6093406).

One would have been motivated to use known sterilizing techniques, such as filter-sterilization, for the advantage of avoiding the effects of contamination. See, for example, US Patent 5583112 which teaches that adjuvants are filtered through a 0.2 mu nylon mesh filter (EXAMPLE 1).

There would have been a reasonable expectation of success given the underlying techniques are widely known and commonly used by the ordinary artisan, including administration of known adjuvants or NAC as shown by the prior art. Thus, the

invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 1/11/2010 have been fully considered but they are not persuasive. It is noted that the previous rejection contained an incorrect citation and US Patent No. 6416947 should have been cited as US Patent No. 6093406. This mistake has been amended in the rejection above. However, arguments in view of the relevant art applied are addressed below.

Applicant states it can be conclusively determined that the adjuvant used by Ueda et al. was Freund's adjuvant by tracing back through the cited references to Iwai et al., *Neuron*, 14:467-475 (1995); see p. 5 of the appeal brief. Applicant argues that that the Office made an incorrect assumption that Ueda et al. used no adjuvant (p. 7, para. 2). Note that while the teachings of Ueda et al. are silent with respect to which adjuvant(s), if any, was used, this argument is not clear. The use of adjuvants is both widely accepted in immunogenic compositions and commonly used as shown by the prior art above (e.g. alum and QS-21). If Freund's adjuvant was used in the teachings of Ueda et al., it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute one equivalent for another for the same purpose; also see MEPE 2144.06, Art Recognized Equivalence for the Same Purpose, II. SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE. Separately, if no adjuvant was used in the disclosure by Ueda et al, it would have been obvious to one of ordinary skill

in the art at the time of the invention to do so for the advantage of increasing or optimizing an immune response.

Applicant alleges that the assumption that laboratory researchers would voluntarily make an antibody as a research reagent under GMP conditions is implausible (p. 7). Applicant states that GMP regulations are directed to drug manufacturers and not laboratory researchers (p. 7-8). Further, applicant submits that no evidence that GMP conditions have ever been used in a laboratory has been provided (p. 8). In response, it is noted that the claims do not require the composition to be associated with either a laboratory worker or a drug manufacturer. However, applicant's argument is not found persuasive because depending on the *intended use* of the composition, one of ordinary skill in the art would have followed GMP conditions and such conditions are widely taught. *Note that the purpose of vaccine research is to ultimately develop vaccines.* One of ordinary skill in the art would have been motivated to follow such conditions for the advantage of obtaining pure products; see the teachings of US Patent 6172122 disclosing that following GMP conditions would ensure purity, prevent the transmission of biological disease agents and avoid adulteration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims

are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-55 of U.S. Patent No. 6890535. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to either the composition comprising an alpha-synuclein and an adjuvant or the intended use thereof (see claims of '535).

Claims 1, 4 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32-39 of copending Application No. 11/660015 in view of US Patent 5583112. Both sets of claims are drawn to the fragments of alpha-synuclein or the intended use thereof. While the claims of the '015 application do not read upon an adjuvant, US Patent 5583112 describes the immunogen activity of the saponin conjugates and saponin adjuvants, including QS-21 also known as QA-21 (see whole document). It would have been obvious for one of ordinary skill in the art at the time of the invention to further incorporate a known adjuvant in the composition taught by '015 for the advantage of increasing immunogen activity.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
SPE, Art Unit 1648.